UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte BRIAN SEED,
CHARLES ROMEO and WALDEMAR KOLANUS

Appeal No. 2004-1736
Application No. 09/243,008

ON BRIEF

Before MILLS, GRIMES, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 44-47, 51, 52, 72-75, 79, 100 and 101. Claims 44 and 79 are representative of the subject matter on appeal, and read as follows:

> 44. A cell which expresses at least two proteinaceous membrane-bound chimeric receptors,
>
> the first of said receptors comprising (a) an extracellular portion which is capable of specifically recognizing and binding a target cell or a target infective agent, (b) a transmembrane portion derived from a T cell receptor, a B cell receptor, or an Fc receptor protein, which, in the absence of an intracellular signalling domain, is capable of signalling said cell to destroy a receptor-bound target cell or a receptor-bound target infective agent, and (c) an intracellular domain that does not signal said cell to destroy a

receptor-bound target cell or a receptor-bound target infective agent; and

the second of said receptors comprising (a) an extracellular portion which is capable of specifically recognizing and binding said target cell or said target infective agent, and (b) an intracellular portion which is derived from CD28.

79. A cell which expresses at least two proteinaceous membrane-bound chimeric receptors,

the first of said receptors comprising (a) an extracellular portion which is capable of specifically recognizing and binding a target cell or a target infective agent, and (b) a transmembrane portion derived from a T cell receptor CD3, zeta, or eta polypeptide, a B cell receptor, or ab Fc receptor, and (c) an intracellular domain that does not signal target cell or target infective agent destruction; and

the second of said receptors comprising (a) an extracellular portion which is capable of specifically recognizing and binding said target cell or said target infective agent, and (b) an intracellular portion which is derived from CD28.

The examiner does not rely on any references.

Claims 44-47, 51-52, 72-75, 79, 100 and 101 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention. After careful review of the record and consideration of the issues before us, we affirm.

BACKGROUND

According to the Specification,

Although native T cell, B cell, and Fc receptors are or can be highly complicated multimeric structures not lending themselves to convenient manipulation, the present invention demonstrates the feasibility of creating chimeras between the intracellular domain of any variety of molecules which are capable of fulfilling the task of target recognition. In particular, the formation of chimeras

> consisting of the intracellular portion of T cell/Fc receptor zeta, eta, or gamma chains joined to the extracellular portion of a suitably engineered antibody molecule allows the target recognition potential of an immune system cell to be specifically redirected to the antigen recognized by the extracellular antibody portion
>
> .

Page 10, lines 1-14.

The specification discloses further

> Thus, because the intracellular domains of the chimeric receptors mediate the proliferative responses of the cells, the coordination of the extracellular domains by a variety of aggregating stimuli specific for the extracellular domains (e.g., an antibody specific for the extracellular domain) will result in proliferation of the cells bearing the chimeras.

Id. at page 11, lines 26-32.

The inventors envision that cells expressing the chimeric receptors would be useful in treatment of conditions such as HIV. Thus, the specification teaches "[s]pecifically the invention provides for a method of directing cellular response to an HIV-infected cell. The method comprises administering to a patient an effective amount of cytotoxic T lymphocytes, said lymphocytes being capable of specifically recognizing and lysing cells infected with HIV as well as circulating virus." Id. at 13, pages 19-24.

DISCUSSION

Claims 44-47, 51-52, 72-75, 79, 100 and 101 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had

possession of the claimed invention. As the claims stand or fall together, see Appeal Brief, page 5, we focus our analysis on claim 44.

According to the rejection, "[a]pplicant has no support in the originally filed claims or specification for the genus phrase language 'an intracellular domain that does not signal to said cell to destroy a receptor-bound target cell or receptor-bound target infective agent,' present in amended base claims 44 and 79." Examiner's Answer, page 3.

As noted by our reviewing court, the Court of Appeals for the Federal Circuit,

> In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide in haec verba support for the claimed subject matter at issue. Nonetheless, the disclosure must convey with reasonable clarity to those skilled in the art that the inventor was in possession of the invention. Put another way, one skilled in the art, reading the original disclosure, must immediately discern the limitation at issue in the claims. That inquiry is a factual one and must be assessed on a case-by-case basis.

Purdue Pharma v. Faulding Inc., 230 F.2d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) (citations omitted) (emphasis added). We agree with the examiner that the disclosure as originally filed, does not reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Appellants assert that the examiner has conceded that the specification provides a working example of the claimed invention, and that the present claims are not directed to a subgenus that is not described in the specification. See Appeal Brief, page 10. Appellants cite page 48 of the specification, lines 31-33,

which describes a chimera that possesses a transmembrane domain joined to an intracellular domain of only three amino acids, wherein the chimera is capable of signaling through its transmembrane domain. See id. Appellants also cite the declaration of Dr. Brian Seed, which attests to the fact that the three amino acids do not signal, but rather anchor the chimera into the cell membrane, and that signaling is mediated by the transmembrane domain. Appellants conclude that "[a]s [the] specification provides a working example of a chimeric receptor that signals through a transmembrane (and not an intracellular) domain, precisely as specified by the present amended claims, the specification and the claims, prior to the present amendments, clearly included these features; no sub-genus has been created." Id. at 11.

The portion of the specification that appellants cite to states:

> To identify the minimal ζ sequences necessary for cytolysis, a series of deletion mutants were prepared in which successively more of the ζ intracellular domain was removed from the carboxyl terminus (Fig. 8A). Most of the intracellular domain could be removed with little consequence for cytolytic potential; the full length chimera CD16:ζ was essentially equal in efficiency to the chimera deleted to residue 65, CD16:ζAsp66* (Fig. 8B). A substantial decrease in cytotoxicity was observed on deletion to ζ residue 59 (chimera CD16:ζGlu60*), and further deletion to residue 5r0 resulted in slightly less activity. However, complete loss of activity was not observed even when the intracellular domain was reduced to a three residue transmembrane anchor (Fig. 8B).

Specification, page 48, lines 20-33.

On page 18, the specification, however, defines a T cell, B cell, or Fc receptor chimera as "include[ing] any functional derivative, fragments, variants, analogues, or chemical derivatives which may be substantially similar to the 'wild-

type' chimera and which possess similar activity (i.e., most preferably, 90%, more preferably, 70%, preferably 40%, or at least 10% of the wild-type receptor chimera's activity." As can be seen from Figure 8B, however, the activity of chimeric receptor wherein the intracellular domain is a three amino acid is almost negligible, and there is nothing on the record demonstrating that the aforementioned chimera has at least 10% of the wild-type receptor chimera's activity. Thus, one skilled in the art reading the example of the chimera having only a three amino acid anchor in light of the earlier definition of a T cell, B cell, or Fc receptor chimera would not immediately discern that a chimera having "an intracellular domain that does not signal said cell to destroy a receptor-bound target cell or a receptor-bound target infective agent" to be part of the invention, as the examples shown in Figure 8B demonstrate that it is the intracellular domain that primarily allows the chimera to signal the cell to destroy a receptor-bound target cell or a receptor-bound target infective agent.

We also note that claim 44 requires "an intracellular domain that does not signal said cell to destroy a receptor-bound target." A protein domain, as understood by the skilled artisan, is an "independently folded unit" that typically contains between 50 and 300 amino acids. See Darnell et al., Molecular Cell Biology, Second Edition, Scientific American Books, page 50 (1990). Thus, a three amino acid "anchor" would not be construed by the skilled artisan as an "intracellular domain" as required by the claim.

The declaration of Dr. Seed does not remedy the above deficiencies of the specification. All Dr. Seed points out is that "the three amino acid domain of the

chimeric receptor described on page 48, lines 31-33, and Figure 8A . . . does not signal a host cell to destroy a receptor-bound target," but instead "likely functions as an anchor to help hold the chimera in the cell membrane." Declaration of Dr. Brian Seed, May 8, 2002, paragraph 2. But, the specification at page 48 notes as to the chimera referenced by Dr. Seed that there was not a "complete loss of activity," and nothing in the declaration points out how the chimera meets the definition set forth at page 18 of the specification.

Appellants argue further that "amendments made to claims 44 and 79 during the prosecution of the application do no more than highlight the fact that it is the transmembrane domain that signals, and that the intracellular domain does not signal the cell to destroy a receptor-bound target cell or receptor-bound target infective agent." Appeal Brief, page 9. Appellants contend that original claim 44 supports the fact that the transmembrane domain is capable of signaling target destruction, and that alone is sufficient basis to reverse the rejection. See id.

As discussed above, the disclosure as originally filed does not support a claim where it is the intracellular domain is incapable of signaling the cell to destroy a receptor-bound target cell or receptor-bound target infective agent. As to originally filed claim 44, that claim recites:

A cell expressing a proteinaceous membrane-bound chimeric receptor, said receptor comprising (a) an extracellular portion which is capable of specifically recognizing and binding a target cell or a target infective agent, and (b) a transmembrane portion derived from a T cell receptor, a B cell receptor, or an Fc

receptor which is capable of signaling said cell to destroy a receptor-bound target cell or receptor-bound target infective agent.

The above claim, however, as pointed out by the examiner, see Examiner's Answer, page 5, does not provide support for the negative limitation of a chimera having "an intracellular domain that does not signal said cell to destroy a receptor-bound target cell or a receptor-bound target infective agent." As was noted above, the chimeras disclosed at page 48 of the specification and shown in Figures 8A and 8B, the intracellular portions were capable of such signaling. The only chimera that wherein the intracellular portion was not capable of such signaling is the chimera having the three amino acid anchor, and as noted above, that example also does not provide support for the added negative limitation.

Appellants assert further that their "discovery that a transmembrane domain can signal target cell destruction represents an important finding in understanding receptor function and was subsequently published in the scientific literature." Reply Brief, page 8.

While we concede that the above may true, it has no bearing on the issue on appeal, that is, whether the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

CONCLUSION

Because we find that disclosure as filed does not describe the claimed subject matter in such a way as to reasonably convey to one skilled in the art that the inventors at the time the application was filed, had possession of the claimed invention, the rejection is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Demetra J. Mills	)
Administrative Patent Judge	)
	)
	)
	) BOARD OF PATENT
Eric Grimes	)
Administrative Patent Judge	) APPEALS AND
	)
	) INTERFERENCES
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